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Patient Preferences for CDK4/6 Inhibitor Treatments in HR+/HER2− Early Breast Cancer: A Discrete Choice Survey Study

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INTRODUCTION

- The monarchE trial (NCT03155997) investigated the addition of a CDK4/6 inhibitor (CDK4/6i) to adjuvant endocrine therapy (ET), evaluating abemaciclib + ET vs ET alone in patients with hormone receptor–positive (HR+), human epidermal growth factor receptor 2–negative (HER2−) early breast cancer (EBC), focusing only on lymph node (LN)+ high-risk patients[1,2]
  - Abemaciclib was US Food and Drug Administration approved in this indication in 2021[3]
- NATALEE (NCT03701334) evaluated ribociclib + nonsteroidal aromatase inhibitor (NSAI) vs NSAI alone in patients with stage II and III disease, regardless of nodal status[4]
  - NATALEE recently reported a statistically significant invasive disease-free survival (iDFS) benefit with ribociclib[5]
- For patients treated in a curative setting, efficacy and tolerability are both important
- This prospective study evaluated the extent to which patients with EBC value different treatment attributes and how these translate into preferences for 2 CDK4/6is, ribociclib and abemaciclib, in the United States (US)

METHODS

- A web-based discrete choice experiment (DCE) survey was conducted between January and May 2023 before NATALEE results were available
- Eligible patients were adult women in a US clinical practice setting with self-reported stage II or III HR+/HER2− EBC, with or without prior chemotherapy, who were receiving only adjuvant ET at the time of survey, and who completed curative surgery 1-3 years prior to the survey
- Attributes included in the DCE survey were informed by 14 initial qualitative interviews (to identify attributes most relevant to patients), expert clinical input, and differentiating features between both CDK4/6is
  - A total of 8 attributes related to efficacy (5-year iDFS), adverse events, blood tests, electrocardiogram (EKG) monitoring requirements, treatment duration, and schedule were included (**Table 1**)
  - A panel of experts (2 breast oncologists and a patient advocate) informed survey design and attribute selection
- Participants selected the scenario that best reflected their preferences from a series of 10 choice cards, each displaying a pair of hypothetical treatment profiles (**Figure 1**)
- A conditional logistic regression model was used to estimate preference weights. Sensitivity analysis was performed by excluding patients who failed internal validity tests
- Relative importance (RI) of each attribute, minimum acceptable benefit, and overall utility were calculated for the full sample. Subgroup analyses were conducted by BC stage (II vs III) and menopausal status (pre-/peri-menopausal vs post-menopausal)

Table 1. Attributes and Levels

Features	Treatment efficacy	Thromboembolic events	Diarrhea	Fatigue	No. of blood tests	No. of EKGs	Treatment duration	Treatment schedule
Level 1	90 out of 100 (90%)	1 out of 100 (1%)	10 out of 100 (10%)	10 out of 100 (10%)	Every 2 weeks for the first 2 months, monthly for the next **2 months**	**No** EKGs required	**2** years	**Once** daily, **intermittent** treatment with a 1-week break each month
Level 2	85 out of 100 (85%)	3 out of 100 (3%)	75 out of 100 (75%)	40 out of 100 (40%)	Every 2 weeks for the first 2 months, monthly for the next **4 months**	**3 EKGs** in the first month	**3** years	**Twice** daily, **continuous** treatment
Level 3	80 out of 100 (80%)							
Level 4	75 out of 100 (75%)							

Figure 1. Choice Card Examples

Treatment features	Treatment A	Treatment B
A. Treatment efficacy	75 out of 100 (75%)	75 out of 100 (75%)
B. Thromboembolic events	3 out of 100 (3%)	1 out of 100 (1%)
C. Diarrhea	10 out of 100 (10%)	75 out of 100 (75%)
D. Fatigue	40 out of 100 (40%)	40 out of 100 (40%)
E. No. of blood tests	Every 2 weeks for the first 2 months, monthly for the next **4 months**	Every 2 weeks for the first 2 months, monthly for the next **2 months**
F. No. of EKGs	**No** EKGs required	**3** EKGs required
G. Treatment duration	**3** years	**2** years
H. Treatment schedule	**Once daily**, **intermittent** treatment with a 1-week break each month	**Once daily**, **intermittent** treatment with a 1-week break each month
Please tell us which treatment you would prefer	I prefer treatment A ○	I prefer treatment B ○

RESULTS

Patient characteristics

- A diverse group of 409 US-based women participated in the survey (median age, 53 years; White/Black/other race, 59%/23%/23%)
  - 197 patients with stage II BC and 212 with stage III BC
- Patient demographics and clinical characteristics are presented in **Table 2**
  - A high proportion of patients with stage II BC were pre-/peri-menopausal (64.0%), and a high proportion of patients with stage III BC were post-menopausal (65.1%)

Table 2. Patient Characteristics (Overall and by BC Stage Subgroups)

Characteristics	Overall N = 409	Stage	
		Stage II N = 197	Stage III N = 212
Age, mean ± SD [median], years	54.5 ± 7.8 [53.0]	52.6 ± 7.9 [51.0]	56.2 ± 7.3 [56.0]
Race,[a] n (%)			
White or Caucasian	240 (58.7)	122 (61.9)	118 (55.7)
Black or African American	94 (23.0)	41 (20.8)	53 (25.0)
Other/prefer not to answer	92 (22.5)	47 (23.9)	45 (21.2)
Time since first breast cancer diagnosis,[b] n (%)			
<2 years ago	112 (27.4)	76 (38.6)	36 (17.0)
2 years to <3 years ago	165 (40.3)	72 (36.5)	93 (43.9)
3 years to <5 years ago	126 (30.8)	49 (24.9)	77 (36.3)
Menopausal status,[c] n (%)			
Pre-menopausal or peri-menopausal	199 (48.7)	**126 (64.0)**	73 (34.4)
Post-menopausal	209 (51.1)	71 (36.0)	**138 (65.1)**
BC stage,[c] n (%)			
Stage II	197 (48.2)	197 (100.0)	0 (0.0)
Stage III	212 (51.8)	0 (0.0)	212 (100.0)
Type of treatment received in the past,[a] n (%)			
Chemotherapy	286 (69.9)	136 (69.0)	150 (70.8)
Hormonal/estrogen treatment	235 (57.5)	112 (56.9)	123 (58.0)
PARP inhibitors	24 (5.9)	6 (3.0)	18 (8.5)
Not sure	12 (2.9)	0 (0.0)	12 (5.7)
Employment status,[b] n (%)			
Employed	104 (25.4)	52 (26.4)	52 (24.5)
Not working	246 (60.1)	120 (60.9)	126 (59.4)
US census region, n (%)			
Northeast	61 (14.9)	25 (12.7)	36 (17.0)
Midwest	34 (8.3)	13 (6.6)	21 (9.9)
South	104 (25.4)	43 (21.8)	61 (28.8)
West	163 (39.9)	91 (46.2)	72 (34.0)
Prefer not to answer	47 (11.5)	25 (12.7)	22 (10.4)

SD, standard deviation.
[a]Categories are not mutually exclusive. [b]Responses of 'Not sure' and 'Prefer not to answer' are not shown. [c]At survey completion.

Relative importance of attributes

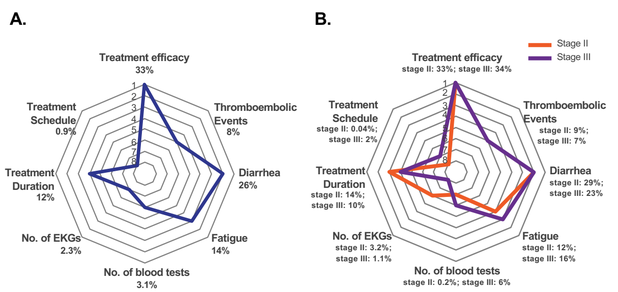
- In order of high to low RI, higher efficacy (iDFS), lower risk of diarrhea, lower risk of fatigue, shorter treatment duration, and lower risk of venous thromboembolic events (VTEs) were of highest RI when making treatment decisions (**Figure 2A**)
  - Number of blood tests in the first 6 months, number of EKGs in the first month, and treatment schedule did not affect patient's choice of treatment
- On average, patients would require at least a 3.5 percentage point improvement in 5-year iDFS to tolerate a 1.9 percentage point increase in the risk of thromboembolic events*
- Additionally, patients would require an 11.2 or 4.0 percentage point increase in 5-year iDFS to tolerate a 62.1 percentage point increase in the risk of diarrhea or a 19.0 percentage point increase in the risk of fatigue, respectively*

* Increased risk based on levels associated with CDK4/6i treatment profiles

Relative importance of attributes in subgroups

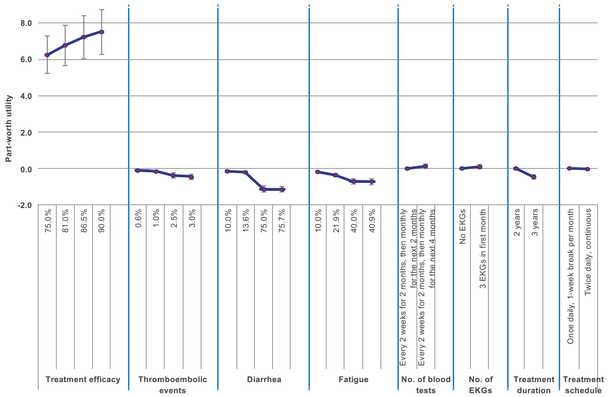
- Subgroup results by stage and menopausal status were generally consistent with the overall sample (**Figure 2B**)
  - One exception is that duration of treatment ranked relatively higher than fatigue in the stage II and pre-menopausal subgroups (results shown only by stage in Figure 2B)

Figure 2. Relative Importance of Each Attribute in the Overall Sample (A) and by BC Stage (B)



Note:
1. This radar chart demonstrates the RI of each attribute, with 1 being the highest RI and 8 the lowest RI.
2. Subgroup lines (orange and purple) are not shown where the results are consistent with the full sample.

Figure 3. Part-Worth Utilities (N = 409)



Note:
1. Solid line represents the range of levels assessed in the DCE choice cards; dotted line represents levels beyond the range assumed for ribociclib or abemaciclib treatment profiles.

Treatment profile utility scores

- Overall utility scores were consistently higher for reconstructed treatment profiles that resembled ribociclib features, including under conservative scenarios where efficacy of ribociclib was assumed to be equivalent to or lower than that of abemaciclib (**Figure 3**)
  - The difference in utility score was primarily driven by differences in the risk of diarrhea, efficacy, and fatigue, respectively

Limitations

- Participant eligibility for the survey was determined based on self-reported information, which may be subject to recall bias
- To reduce the response burden, this study did not consider all possible treatment attributes; other attributes may impact patients' preferences
- DCE relies on the assumption that participants make rational choices. Sensitivity analyses were conducted to demonstrate robustness of results

KEY FINDINGS & CONCLUSIONS

- This DCE surveyed 409 patients with stage II and III HR+/HER2− EBC from the US on key treatment attributes, mainly identified by qualitative interviews of patients, that may influence their treatment preference for a CDK4/6i in the adjuvant setting
  - Higher efficacy, lower risk of diarrhea, lower risk of fatigue, shorter treatment duration, and lower risk of VTEs were of highest RI when making treatment decisions
  - Thus, patients with HR+/HER2− EBC have a strong preference for treatment profiles that maximize efficacy while minimizing symptomatic adverse events
- Based on the reconstructed utility scores, on average, patients in this study favor treatment profiles that more closely resemble ribociclib
- These patient preferences are critical for shared treatment decision-making when discussing adding a CDK4/6i to adjuvant ET treatment for eligible patients with HR+/HER2− EBC

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